REMARKS

This is in response to the Official Action mailed February 3, 2004 for the above-identified application. Further to the Examiner's restriction requirement, Claims 1-3, 5-12, 23-29, 32, and 34-35 have been withdrawn. Applicants reserve the right to prosecute non-elected subject and cancelled subject matter in separate applications. Applicants have elected with traverse Claims 4, 13, 14, 16, 18-22, 30, 31 and 33. Claims 4 and 13 have been amended to correct minor informalities as is further described below.

Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 have been rejected under 35 USC 112, first paragraph as allegedly not enabled by the specification. As a preliminary matter, Applicants note that the Examiner states (Official Action, page 3, second full paragraph) that the ground of rejection targets "the compositions in which growth hormone is not present." In this regard, Applicants respectfully point out that all pending claims require a growth hormone, which is recited in independent claim 4.

The Examiner states that "the fact that an assay can be conducted does not mean that any particular result will be obtained," and alleges that "where receptor activation and inhibition is concerned, structure/activity relationships are unpredictable." Official Action, page 3, third full paragraph, last two sentences). The Examiner also selectively provides references that allegedly support a conclusion that "one cannot 'predict' whether, or the extent to which, a given compound will activate a receptor, or antagonize it; (b) even if one can show that receptor activation or antagonism occurs in vitro, such a result is not necessarily predictive of what will happen *in vivo*." Official Action, page 5, first full paragraph, first sentence. The Examiner further states that "[e]ven the fact that a claim in a U.S. Patent is drawn to a given compound does not mean that evidence of enablement has been provided in that patent (notwithstanding the presumption of validity that is conferred upon all U.S. patents)." Official Action, page 6, lines 1-4. The Examiner also alleges that based on the *In re Wands* factors, "undue experimentation" would be required; however, the Examiner does not provide an analysis of the *In re Wands* factors on which to base his conclusion. The Examiner also takes the position that the term "pharmaceutical" should be deleted from the claims because "there is no evidence that the compounds which are asserted in claim 4 ... do in fact antagonize CRF receptors," and that "even if [such] evidence were provided, this would not amount to evidence of therapeutic efficacy ... *in vivo*". Official

Action, page 7, lines 9-15.

In addition to the aforestated reasons, reiterated here, for withdrawing the rejection, Applicants respectfully submit that Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 are enabled by the specification and that the rejection under 35 USC 112 is for these additional reasons therefore further improper. The Examiner repeatedly emphasizes the lack of evidence of efficacy *in vivo*. However, evidence of *in vivo* activity is not required for patentability. For example, an Applicant does not have to provide "that a correlation exists between a particular activity and an asserted therapeutic use of a compound..." MPEP 2107.03, section I. In addition, "in no case has a Federal Court required an applicant to support an asserted utility with data from human clinical trials." MPEP 2107.03, section III. Moreover, "absolute certainty [of the operability of an invention] is not required by law." *Id.* (citing *In re Wooddy,* 331 F.2d 636, 639 (CCPA 1964)). Accordingly, the Examiner has inappropriately placed on the Applicant a burden of proof that the law does not require.

In addition, even the references cited by the Examiner do not lead to the conclusion that the pending claims are not enabled. The Examiner states, for example, that McFadyen discloses that potency changes "did not *always* correlate with affinity" (Official Action, page 4, first paragraph); that receptor activation "is not *necessarily* predictive of *in vivo* activity" according to Xiao (Official Action, page 4, third paragraph); that receptor activation and the subsequent biological response "is not determined *solely* by binding affinity" according to Lunec (Official Action, page 4, fourth paragraph) (emphasis added in each case). The Examiner's own statements show that one might conclude, *arguendo,* in a worst case scenario for the applicant, that the applicant has not shown absolute certainty of the enablement of the present invention. However, as noted above, "absolute certainty ... is not required by law." *In re Wooddy,* 331 F.2d at 639. The Applicant need only provide "a reasonable correlation between the activity in question and the asserted utility." MPEP 2107.3, section I (citing *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980)) (emphasis in original).

It is respectfully submitted that a reasonable correlation is provided, *inter alia,* by the issued U.S. patents to both CRF antagonists (CRFA) and growth hormone secretagogues (GHS) that are cited in the specification (pages 1-3), and incorporated by reference therein (*see,* e.g., page 3, lines 16-19). It is also respectfully submitted that, the issued U.S. patents to

both CRF antagonists (CRFA) and growth hormone secretagogues (GHS) provide an enabling disclosure that satisfies the requirements of 35 U.S.C. 112, first paragraph, notwithstanding the Examiner's assertion on page 6, lines 1-4 of the Official Action. In particular, the Official Action takes the position, as noted above, that "[e]ven the fact that a claim in a U.S. Patent is drawn to a given compound does not mean that evidence of enablement has been provided in that patent (notwithstanding the presumption of validity that is conferred upon all U.S. patents)." Applicants respectfully remind the Examiner that the "presumption" of validity of a U.S. patent, as repeatedly held in the Court of Appeals for the Federal Circuit, means that the standard required to invalid a U.S. patent is decidedly high: *clear and convincing evidence* (emphasis added). *Geneva Pharmaceuticals, Inc. v. Glaxosmithkline PLC,* 349 F.3d 1373, 1377 (Fed. Cir. 2003); *AK Steel Corp. v. Sollac and Ugine,* 344 F.3d 1234, 1238-39 (Fed. Cir. 2003); and *Cordis Corp. v. Medtronic Ave, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003) are just some of the recent cases reaffirming this standard. This standard is based in no small measure on the belief that the U.S. Patent and Trademark Office is well situated to check what is enabling and what is not; in this regard, the Official Action is not well understood. It is respectfully submitted that the Official Action, by stating that "...the fact that a claim in a U.S. Patent is drawn to a given compound does not mean that evidence of enablement has been provided in that patent...", mistakenly places a burden on the applicant to show that a patent provides evidence of enablement, *.i.e.,* to show that the issued patent is valid. On the contrary, it is the Official Action who has to describe, by *clear and convincing evidence*, in what way the disclosure of issued U.S. patents, incorporated by reference in the specification of the present application, is *not* enabling. The clear and convincing evidence standard entails a high burden of proof, which clearly has not been met in the instant case.

Similar conclusions apply to the term "pharmaceutical," which according to the Official Action should be deleted from the claims because "there is no evidence that the compounds which are asserted in claim 4 ... do in fact antagonize CRF receptors." Once again, the disclosure of issued U.S. patents, incorporated by reference in the specification of the present application, is enabling with regard to the CRF antagonist activity of the compounds. Absent clear and convincing evidence against the validity of the patents at issue, the Examiner's rejection is inappropriate. Indeed, the Official Action, as discussed below, cites issued U.S. Patents as the basis for an obviousness rejection under 35 U.S.C. 103.

Accordingly, the very premise upon which the non-enablement rejection is admittedly based is incorrect and removal of the entire rejection on this basis is requested. In particular, the rejection is internally inconsistent with official allegations subsequently made. The Official Action first alleges that certain compound components are not enabled to justify the rejection under 35 USC 112, first paragraph. However, it then cites various references showing like components for the purported purpose of substantiating an obviousness rejection under 35 U.S.C. 103. But this presumes that the references cited for the purposes of 35 U.S.C. 103 are enabled. Clearly, the Official Action cannot have it both ways.

In summary, in view of the foregoing remarks, Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 are enabled by the specification. Withdrawal of the rejection under 35 USC 112, first paragraph of these claims as allegedly not enabled is respectfully requested.

Claim 4 has been rejected under 35 USC 112, second paragraph as allegedly indefinite due to the recitation of "O" instead of "0." It is respectfully submitted that the recitation of "O" instead of "0" represented a mere typographical error. The claim has been amended to correct every occurrence of this informality. Claim 13 has been similarly amended.

Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 have been rejected under 35 USC 103 as allegedly obvious over Carpino (U.S. Patent No. 6,107,306) in view of Chen '989 (U.S. Patent No. 6,432,989). According to the Examiner, Carpino discloses the treatment of sleep disorders using GHS's but does not suggest combining a GHS with a CRFA. According to the Examiner, Chen '989 discloses the treatment of sleep disorders but does not suggest combining a GHS with a CRFA. The Examiner reaches the conclusion that one skilled in the art would have been motivated to combine Chen '989 with Carpino to obtain additive effects (Official Action, page 9, lines 1-8).

Applicants submit that, if the Official Action persists in the rejection under 35 U.S.C. 112, first paragraph, the obviousness rejection must, for consistency, be withdrawn. Moreover, it is respectfully submitted that Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 are nonobvious and patentable over Carpino in view of Chen '989. To begin with, the Examiner's own statements that "Carpino does not suggest combining a GHS with a CRFA" (Official Action, page 9, line 4) and that "Chen '989 does not suggest combining a GHS with a CRFA" (Official Action, page 9, line 6) concede the impropriety of this rejection. The fact that the Official Action openly admits this means that there is no hint or motivation to

combine the cited references necessary to sustain the rejection. The mere fact that references *can* be combined does not render the combination obvious unless the prior art also suggests the desirability of the combination. MPEP 2143.01 (citing *In re Mills,* 916 F.2d 680 (Fed. Cir. 1990). In this case, the Examiner has indicated that neither reference suggests the desirability of the combination of a GHS with a CRFA. Accordingly, the invention cannot be considered obvious over Carpino in view of Chen '989. Withdrawal of the rejection is therefore requested.

In addition, it is respectfully submitted that, in light of the provisions of 35 U.S.C. 103(c), the combination of Carpino and Chen '989 is improper because neither reference is prior art. In particular, the present application is entitled to a priority date of April 13, 2000, which is the filing date of U.S. Provisional Application Ser. No. 60/196,698, from which the present application claims priority. Carpino issued on August 22, 2000, and Chen '989 issued on August 13, 2003. Therefore, both references issued after April 13, 2000, and therefore neither reference is prior art under either 35 U.S.C. 102(a) or 35 U.S.C. 102(b). In addition, neither 35 U.S.C. 102(c) nor 35 U.S.C. 102(d) is applicable to the present application. Even assuming that Carpino and Chen '989 are prior art under 35 U.S.C. 102(e) or 35 U.S.C. 102(g), 35 U.S.C. 103(c) clearly states that "subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person." In this case, it is respectfully submitted that, at the time the present invention was made, the inventor was an employee of Pfizer Inc. and the present invention was subject to an obligation of assignment to Pfizer, Inc., which is the assignee of record for both cited references. Since Carpino and Chen '989 qualify as prior art only, if at all, under subsections (e) or (g) of section 102, the combination of Carpino with another reference, or of Chen '989 with another reference, does not preclude patentability of this invention.

In view of the foregoing, it is respectfully submitted that the combination of Carpino and Chen '989 does not preclude patentability of Claims 4, 13, 14, 16, 18-22, 30, 31 and 33. Accordingly, withdrawal of the rejection of Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 under 35 U.S.C. 103 as allegedly obvious over Carpino in view of Chen '989 is respectfully requested.

Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 have been rejected under 35 USC 103 as allegedly obvious over Carpino (U.S. Patent No. 6,107,306) in view of Chen '479 (U.S. Patent No. 5,962,479). According to the Examiner, Carpino discloses the treatment of Alzheimer's disease using GHS's but does not suggest combining a GHS with a CRFA. According to the Examiner, Chen '479 discloses the treatment of Alzheimer's disease but does not suggest combining a GHS with a CRFA. The Examiner reaches the conclusion that one skilled in the art would have been motivated to combine Chen '479 with Carpino to obtain additive effects (Official Action, page 9, lines 16-17).

However, it is respectfully submitted that Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 are nonobvious and patentable over Carpino in view of Chen '479 for the same reasons stated immediately above. In brief: the Official Action's admission that there is no relevant suggestion to combine the references causes the obviousness rejection to fail in the first instance. In addition, Carpino is not citable as prior art as discussed above.

In view of the foregoing, it is respectfully submitted that the combination of Carpino and Chen '989 does not preclude patentability of Claims 4, 13, 14, 16, 18-22, 30, 31 and 33. Accordingly, withdrawal of the rejection of Claims 4, 13, 14, 16, 18-22, 30, 31 and 33 under 35 U.S.C. 103 as allegedly obvious over Carpino in view of Chen '989 is respectfully requested.

The Examiner has noted that certain references were not considered as they were not in English. Accordingly, Applicants submit herewith an Information disclosure statement for consideration by the Examiner that lists six U.S. patents and an English language abstract that correspond to the references at issue. Copies of the patents and of the abstract are also enclosed.

In view of the foregoing, examination and allowance of all pending claims is respectfully requested.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

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